EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	6487	"HMG-CoA reductase"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/02/25 09:28
L2	48270	"viral infection"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/02/25 09:28
L3	607	L1 and L2	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/02/25 09:32
L4	9656	lovastatin or simvastatin or fluvastatin or atorvastatin or pravastatin or mevastatin	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/02/25 09:29
L5	1165	L2 and L4	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/02/25 09:30
L6	6907	"respiratory syncytial virus"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/02/25 09:30
L7	37	L1 and L6	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/02/25 09:31

EAST Search History

L8	168	L4 and L6	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/02/25 09:34

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NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
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NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 26	FEB 13	CASREACT coverage to be extended
NEWS 27	Feb 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 28	Feb 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 29	Feb 23	KOREAPAT enhanced with IPC 8 features and functionality

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
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=> s HMG-CoA reductase
L1       27234 HMG-COA REDUCTASE

=> s HMG CoA reductase
L2       27234 HMG COA REDUCTASE

=> s L1 or L2
L3       27234 L1 OR L2

=> s viral or virua
L4      973785 VIRAL OR VIRUA

=> s viral or virus
L5     2314968 VIRAL OR VIRUS

=> s L3 and L5
L6         390 L3 AND L5

=> dup rem L6
PROCESSING COMPLETED FOR L6
L7          278 DUP REM L6 (112 DUPLICATES REMOVED)

=> s respiratory syncytial virus
L8       23351 RESPIRATORY SYNCYTIAL VIRUS

=> s L7 and L8
L9           4 L7 AND L8

=> s parainfluenza or ebola or measles or canine distemper or Newcastles disease
virus or RSV or rhinotracheitis
L10      89256 PARAINFLUENZA OR EBOLA OR MEASLES OR CANINE DISTEMPER OR NEWCAST
               LES DISEASE VIRUS OR RSV OR RHINOTRACHEITIS

=> s L7 and L10
L11          4 L7 AND L10
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=> s L9 or L11
L12          4 L9 OR L11

=> s lovastatin or simvastatin or fluvastatin or atorvastatin or pravastatin or
mevastatin
L13      51648 LOVASTATIN OR SIMVASTATIN OR FLUVASTATIN OR ATORVASTATIN OR
               PRAVASTATIN OR MEVASTATIN

=> s L8 or L10
L14      98668 L8 OR L10

=> s L13 and L14
L15         52 L13 AND L14

=> dup rem L15
PROCESSING COMPLETED FOR L15
L16          34 DUP REM L15 (18 DUPLICATES REMOVED)

=> s L16 (AY<2002 or PRY<2002 or PR<2002)
MISSING OPERATOR 'L80 (AY<2002'
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'2002' NOT A VALID FIELD CODE
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'2002' NOT A VALID FIELD CODE
'2002' NOT A VALID FIELD CODE
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L17          12 L16 AND (AY<2002 OR PRY<2002 OR PY<2002)

=> d L12 1-4 ibib abs

L12  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2002:755195  CAPLUS
DOCUMENT NUMBER:          137:273169
TITLE:                    Method of inhibiting viral infection using
                          HMG-CoA reductase
                          inhibitors and isoprenylation inhibitors
INVENTOR(S):              Graham, Barney Scott; Gower, Tara L.; Pastey, Manoj K.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 24 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     US 2002142940         A1    20021003    US 2001-981682           20011016
PRIORITY APPLN. INFO.:                       US 2000-241247P      P   20001017
AB   Applicants provide methods of inhibiting viral infections, and
     treating an infected individual with AIDS, respiratory
     syncytial virus infection, parainfluenza
     virus infection, and other viral infections.  Inhibitors
     of Rho isoprenylation are used to inhibit Rho cell surface attachment,
     thereby inhibiting the use, by viruses, of Rho as a receptor for
     infection of susceptible cells.  Isoprenylation inhibitors include
     inhibitors specific for the enzymes farnesyltransferase and
     geranylgeranyltranferase, as well as inhibitors of general cholesterol
```

biosynthesis, such as HMG-CoA reductase inhibitors. Mice were treated with 1 mg/day lovastatin, 50 mg/day gemfibrozil, or PBS by oral gavage beginning three days prior to infection with either RSV or vaccinia virus. Vaccinia replication and illness was not effected by lovastatin or gemfibrozil treatment compared to PBS treated controls. Gemfibrozil and PBS treated mice infected with RSV had a peak titer in the lung of 6.5+/-0.43 (log10 pfu/gm) and 6.5+/-0.19 (log10 pfu/gm), resp., while RSV replication in lovastatin treated mice was reduced by nearly 100-fold to 4.7+/-0.4 (log10 pfu/gm).

L12 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:321371 CAPLUS
DOCUMENT NUMBER: 135:150874
TITLE: RhoA Is Activated During Respiratory Syncytial Virus Infection
AUTHOR(S): Gower, Tara L.; Peeples, Mark E.; Collins, Peter L.; Graham, Barney S.
CORPORATE SOURCE: Department of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA
SOURCE: Virology (2001), 283(2), 188-196
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Respiratory syncytial virus (RSV) is an important human pathogen that can cause severe and life-threatening respiratory infections in infants and immunocompromised adults. The authors have recently shown the RSV F glycoprotein, which mediates viral fusion and entry, interacts with the cellular protein RhoA in two-hybrid and in vitro binding assays. Whether this interaction occurs in living cells remains an open question. However, because RhoA signaling is associated with many cellular functions relevant to RSV pathogenesis such as actin cytoskeleton organization, expression of proinflammatory cytokines, and smooth muscle contraction, the authors asked whether RhoA activation occurred during RSV infection of HEp-2 cells. They found that the amount of isoprenylated and membrane-bound RhoA in RSV-infected cultures was increased. Further evidence of RhoA activation was demonstrated by downstream signaling activity mediated by RhoA. There was an increase in p130cas phosphorylation during RSV infection, which was prevented by Y-27632, a specific inhibitor of Rho kinase, or lovastatin, an HMG -CoA reductase inhibitor that reduces the synthesis of groups needed for isoprenylation. In addition, RSV infection of HEp-2 cells resulted in an increase in the formation of actin stress fibers. Pretreatment of HEp-2 cells with Clostridium botulinum C3 exotoxin, an enzyme that specifically ADP-ribosylates and inactivates RhoA, prevented RSV-induced stress fiber formation. Thus, RhoA and subsequent downstream signaling events are activated during RSV infection, which has implications for RSV pathogenesis. (c) 2001 Academic Press.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:121345 CAPLUS
DOCUMENT NUMBER: 126:126927
TITLE: Stable copper(I) complexes as active therapeutic substances
INVENTOR(S): Pallenberg, Alexander J.; Branca, Andrew; Marschner, Thomas M.; Patt, Leonard M.
PATENT ASSIGNEE(S): Procyte Corporation, USA; Pallenberg, Alexander J.; Branca, Andrew; Marschner, Thomas M.; Patt, Leonard M.

SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639144	A1	19961212	WO 1996-US10122	19960606
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9662748	A	19961224	AU 1996-62748	19960606
PRIORITY APPLN. INFO.:			US 1995-468645 A	19950606
			WO 1996-US10122 W	19960606

AB Stable Copper(I) complexes and methods relating thereto are disclosed. The stable Copper (I) complexes comprise a Copper(I) ion complexed by a multi-dentate ligand which favors the +1 oxidation state for copper. The complexes may be used as wound healing agents, anti-oxidative agents, anti-inflammatory agents, lipid modulating agents, signal transduction modulating agents, hair growth agents, and antiviral agents. Uses of this invention also include inhibition of viral infection, as well as inhibiting transmission of sexually transmitted diseases. The stable Copper(I) complexes of the invention include neocuproine Copper(I) and bathocuproine disulfonic acid Copper(I). Preparation of copper (I) neocuproine is described, as are inhibitory effects of the complexes of the invention against e.g a variety of viruses.

L12 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:194941 BIOSIS
DOCUMENT NUMBER: PREV200100194941
TITLE: Antiviral activity of lovastatin against respiratory syncytial virus in vivo and in vitro.
AUTHOR(S): Gower, Tara L.; Graham, Barney S. [Reprint author]
CORPORATE SOURCE: Vanderbilt University School of Medicine, 1161 21st Ave. South, A-4103 MCN, Nashville, TN, 37232-2582, USA
bgraham@mail.nih.gov
SOURCE: Antimicrobial Agents and Chemotherapy, (April, 2001) Vol. 45, No. 4, pp. 1231-1237. print.
CODEN: AMACCQ. ISSN: 0066-4804.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Apr 2001
Last Updated on STN: 18 Feb 2002

AB Respiratory syncytial virus (RSV) is an important human pathogen that can cause severe and life-threatening respiratory infections in infants and immunocompromised adults. We have recently shown that the RSV F glycoprotein, which mediates viral fusion, binds to RhoA. One of the steps in RhoA activation involves isoprenylation at the carboxy terminus of the protein by geranylgeranyltransferase. This modification allows RhoA to be attached to phosphatidyl serine on the inner leaflet of the plasma membrane. Treatment of mice with lovastatin, a drug that inhibits prenylation pathways in the cell by directly inhibiting hydroxymethylglutaryl coenzyme A reductase, diminishes RSV but not vaccinia virus replication when administered up to 24 h after RSV infection and decreases virus-induced weight loss and illness in mice. The inhibition of replication is not likely due to the inhibition of cholesterol biosynthesis, since gemfibrozil, another cholesterol-lowering

agent, did not affect virus replication and serum cholesterol levels were not significantly lowered by lovastatin within the time frame of the experiment. Lovastatin also reduces cell-to-cell fusion in cell culture and eliminates RSV replication in HEp-2 cells. These data indicate that lovastatin, more specific isoprenylation inhibitors, or other pharmacological approaches for preventing RhoA membrane localization should be considered for evaluation as a preventive antiviral therapy for selected groups of patients at high risk for severe RSV disease, such as the institutionalized elderly and bone marrow or lung transplant recipients.

=> d L17 1-12 ibib abs

L17 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:755195 CAPLUS
DOCUMENT NUMBER: 137:273169
TITLE: Method of inhibiting viral infection using HMG-CoA reductase inhibitors and isoprenylation inhibitors
INVENTOR(S): Graham, Barney Scott; Gower, Tara L.; Pastey, Manoj K.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 24 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002142940	A1	20021003	US 2001-981682		20011016 <--
PRIORITY APPLN. INFO.:			US 2000-241247P	P	20001017 <--

AB Applicants provide methods of inhibiting viral infections, and treating an infected individual with AIDS, respiratory syncytial virus infection, parainfluenza virus infection, and other viral infections. Inhibitors of Rho isoprenylation are used to inhibit Rho cell surface attachment, thereby inhibiting the use, by viruses, of Rho as a receptor for infection of susceptible cells. Isoprenylation inhibitors include inhibitors specific for the enzymes farnesyltransferase and geranylgeranyltranferase, as well as inhibitors of general cholesterol biosynthesis, such as HMG-CoA reductase inhibitors. Mice were treated with 1 mg/day lovastatin, 50 mg/day gemfibrozil, or PBS by oral gavage beginning three days prior to infection with either RSV or vaccinia virus. Vaccinia replication and illness was not effected by lovastatin or gemfibrozil treatment compared to PBS treated controls. Gemfibrozil and PBS treated mice infected with RSV had a peak titer in the lung of 6.5+/-0.43 (log10 pfu/gm) and 6.5+/-0.19 (log10 pfu/gm), resp., while RSV replication in lovastatin treated mice was reduced by nearly 100-fold to 4.7+/-0.4 (log10 pfu/gm).

L17 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:521462 CAPLUS
DOCUMENT NUMBER: 137:88442
TITLE: Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms
INVENTOR(S): Shanahan-Pendergast, Elisabeth
PATENT ASSIGNEE(S): Ire.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053138	A2	20020711	WO 2002-IE1	20020102 <--
WO 2002053138	A3	20020919		
W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG				
AU 2002219472	A1	20020716	AU 2002-219472	20020102 <--
EP 1351678	A2	20031015	EP 2002-727007	20020102 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004092583	A1	20040513	US 2004-250535	20040102 <--
PRIORITY APPLN. INFO.:			IE 2001-2 A	20010102 <--
			WO 2002-IE1 W	20020102

OTHER SOURCE(S): MARPAT 137:88442

AB The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixture showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis.

L17 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:838805 CAPLUS

DOCUMENT NUMBER: 136:128604

TITLE: Spontaneous reports on drug-induced pancreatitis in Denmark from 1968 to 1999

AUTHOR(S): Andersen, Vibeke; Sonne, Jesper; Andersen, Morten

CORPORATE SOURCE: Medical Department, Viborg County Hospital, Viborg, 8800, Den.

SOURCE: European Journal of Clinical Pharmacology (2001), 57(6-7), 517-521
CODEN: EJCPAS; ISSN: 0031-6970

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Objectives: To present an update on drug-induced pancreatitis reported to the Danish Committee on Adverse Drug Reactions. Design: Retrospective study of spontaneous case reports to the Danish reporting system on adverse drug reactions. Methods: All cases of suspected drug-induced pancreatitis reported to the Danish Committee on Adverse Drug Reactions from 1968 to 1999 were analyzed. Three cases were excluded leaving 47 cases for anal. Results: Drug-induced pancreatitis made up 0.1% of all the reports to the committee from 1968 to 1999. The proportion seemed to increase and was 0.3% during the last 8 yr. The 47 cases corresponded to 0.1% of the number of patients discharged due to pancreatic disease (without cancers) per yr in Denmark. Serious courses were frequent as indicated by death and hospitalization being reported in 4 (9%) and 32 (68%) cases, resp. Death occurred after valproate (two cases), clomipramine (one case) and azathioprine (one case). Definite relationship was stated for mesalazine (three cases), azathioprine (two cases) and simvastatin (one case) on the basis of re-challenge. A possible or probable causality was considered for a further 30 drugs including 5-acetylsalicylic acid agents, angiotensin-converting enzyme inhibitors, estrogen prepns., didanosine, valproate, codeine, antiviral agents used in acquired immunodeficiency syndrome therapy, various lipid-reducing agents, interferon, paracetamol, griseofulvin, ticlopidine, allopurinol, lithium and the MMR (measles/mumps/rubella) vaccination. Conclusion: Drug-induced pancreatitis is rarely reported. The incidence may be

increasing and the course is often serious. This is the first report on definite simvastatin-induced pancreatitis. Further studies on the pancreotoxic potential of drugs are warranted.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:321371 CAPLUS
DOCUMENT NUMBER: 135:150874
TITLE: RhoA Is Activated During Respiratory Syncytial Virus Infection
AUTHOR(S): Gower, Tara L.; Peeples, Mark E.; Collins, Peter L.; Graham, Barney S.
CORPORATE SOURCE: Department of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA
SOURCE: Virology (2001), 283(2), 188-196
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Respiratory syncytial virus (RSV) is an important human pathogen that can cause severe and life-threatening respiratory infections in infants and immunocompromised adults. The authors have recently shown the RSV F glycoprotein, which mediates viral fusion and entry, interacts with the cellular protein RhoA in two-hybrid and in vitro binding assays. Whether this interaction occurs in living cells remains an open question. However, because RhoA signaling is associated with many cellular functions relevant to RSV pathogenesis such as actin cytoskeleton organization, expression of proinflammatory cytokines, and smooth muscle contraction, the authors asked whether RhoA activation occurred during RSV infection of HEp-2 cells. They found that the amount of isoprenylated and membrane-bound RhoA in RSV-infected cultures was increased. Further evidence of RhoA activation was demonstrated by downstream signaling activity mediated by RhoA. There was an increase in p130cas phosphorylation during RSV infection, which was prevented by Y-27632, a specific inhibitor of Rho kinase, or lovastatin, an HMG-CoA reductase inhibitor that reduces the synthesis of groups needed for isoprenylation. In addition, RSV infection of HEp-2 cells resulted in an increase in the formation of actin stress fibers. Pretreatment of HEp-2 cells with Clostridium botulinum C3 exotoxin, an enzyme that specifically ADP-ribosylates and inactivates RhoA, prevented RSV-induced stress fiber formation. Thus, RhoA and subsequent downstream signaling events are activated during RSV infection, which has implications for RSV pathogenesis. (c) 2001 Academic Press.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:300514 CAPLUS
DOCUMENT NUMBER: 134:331617
TITLE: Oil-in-water emulsion compositions for polyfunctional active ingredients
INVENTOR(S): Chen, Feng-jing; Patel, Mahesh V.
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001028555	A1	20010426	WO 2000-US28835	20001018 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002107265	A1	20020808	US 1999-420159	19991018 <--
US 6720001	B2	20040413		
PRIORITY APPLN. INFO.:			US 1999-420159 A	19991018 <--

AB Pharmaceutical oil-in-water emulsions for delivery of polyfunctional active ingredients with improved loading capacity, enhanced stability, and reduced irritation and local toxicity are described. Emulsions include an aqueous phase, an oil phase comprising a structured triglyceride, and an emulsifier. The structured triglyceride of the oil phase is substantially free of triglycerides having three medium chain (C6-C12) fatty acid moieties, or a combination of a long chain triglyceride and a polarity-enhancing polarity modifier. The present invention also provides methods of treating an animal with a polyfunctional active ingredient, using dosage forms of the pharmaceutical emulsions. For example, an emulsion was prepared, with cyclosporin A as the polyfunctional active ingredient dissolved in an oil phase including a structured triglyceride (Captex 810D) and a long chain triglyceride (safflower oil). The composition contained (by weight) cyclosporin A 1.0, Captex 810D 5.0, safflower oil 5.0, BHT 0.02, egg phospholipid 2.4, dimyristoylphosphatidyl glycerol 0.2, glycerol 2.25, EDTA 0.01, and water up to 100%, resp.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 12 CAPLUS

ACCESSION NUMBER: 2001:227519 CAPLUS
DOCUMENT NUMBER: 135:28721

TITLE: Antiviral activity of lovastatin against respiratory syncytial virus in vivo and in vitro

AUTHOR(S): Gower, Tara L.; Graham, Barney S.
CORPORATE SOURCE: Departments of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2001), 45(4), 1231-1237
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Respiratory syncytial virus (RSV) is an important human pathogen that can cause severe and life-threatening respiratory infections in infants and immunocompromised adults. We have recently shown that the RSV F glycoprotein, which mediates viral fusion, binds to RhoA. One of the steps in RhoA activation involves isoprenylation at the carboxy terminus of the protein by geranylgeranyltransferase. This modification allows RhoA to be attached to phosphatidyl serine on the inner leaflet of the plasma membrane. Treatment of mice with lovastatin, a drug that inhibits prenylation pathways in the cell by directly inhibiting hydroxymethylglutaryl CoA reductase, diminishes RSV but not vaccinia virus replication when administered up to 24 h after RSV infection and decreases virus-induced weight loss and illness in mice. The inhibition of replication is not likely due to the inhibition of cholesterol biosynthesis, since gemfibrozil, another cholesterol-lowering

agent, did not affect virus replication and serum cholesterol levels were not significantly lowered by lovastatin within the time frame of the experiment Lovastatin also reduces cell-to-cell fusion in cell culture and eliminates RSV replication in HEp-2 cells. These data indicate that lovastatin, more specific isoprenylation inhibitors, or other pharmacol. approaches for preventing RhoA membrane localization should be considered for evaluation as a preventive antiviral therapy for selected groups of patients at high risk for severe RSV disease, such as the institutionalized elderly and bone marrow or lung transplant recipients.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:259972 CAPLUS
DOCUMENT NUMBER: 132:293042
TITLE: Encapsulation of sensitive liquid components into a matrix to obtain discrete shelf-stable particles
INVENTOR(S): Van Lengerich, Bernhard H.
PATENT ASSIGNEE(S): General Mills, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000021504	A1	20000420	WO 1999-US20905		19991006 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2345815	A1	20000420	CA 1999-2345815		19991006 <--
AU 9963872	A1	20000501	AU 1999-63872		19991006 <--
AU 777977	B2	20041104			
EP 1119345	A1	20010801	EP 1999-951433		19991006 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002527375	T	20020827	JP 2000-575480		19991006 <--
PRIORITY APPLN. INFO.:			US 1998-103700P	P	19981009 <--
			US 1998-109696P	P	19981124 <--
			US 1999-233443	A	19990120 <--
			WO 1999-US20905	W	19991006 <--

AB A liquid encapsulant component which contains an active, sensitive encapsulant, such as a live microorganism or an enzyme dissolved or dispersed in a liquid plasticizer is admixed with a plasticizable matrix material. The matrix material is plasticizable by the liquid plasticizer and the encapsulation of the active encapsulant is accomplished at a low temperature and under low shear conditions. The active component is encapsulated and/or embedded in the plasticizable matrix component or material in a continuous process to produce discrete, solid particles. The liquid content of the liquid encapsulant component provides substantially all or completely all of the liquid plasticizer needed to plasticize the matrix component to obtain a formable, extrudable, cuttable, mixture or dough. Removal of liquid plasticizer prior to extrusion is not needed to adjust the viscosity of the mixture for formability. Release of an active component from the matrix may be delayed or controlled over time so that the active component is delivered when and where it is needed to perform

its intended function. Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:291059 CAPLUS
DOCUMENT NUMBER: 122:75939
TITLE: Madin Darby bovine kidney cell synchronization by lovastatin: Application to bovine herpesvirus-1 gene expression
AUTHOR(S): Vanderplasschen, A.; Hanon, E.; Benarafa, C.; Greimers, R.; Beeck, A Op De; Loncar, M.; Pastoret, P P.
CORPORATE SOURCE: Faculte de Medecine Veterinaire, Universite de Liege, Liege, B-4000, Belg.
SOURCE: Veterinary Research (1994), 25(6), 555-67
CODEN: VEREEM; ISSN: 0928-4249
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The number of investigations involving cell proliferation has increased rapidly in the last years. One of the major difficulties in studying cell-cycle-related events is obtaining highly synchronous cell populations without metabolic imbalance. This study demonstrates that the Madin Darby bovine kidney (MDBK) cells, a commonly used cell line in veterinary research, can be effectively synchronized using lovastatin (Lov), a drug used to treat hypercholesteremia in humans. This was demonstrated by the following results: (i) Lov inhibits cell proliferation in a dose-dependent manner; (ii) Lov synchronizes MDBK cells mainly in the G1 and secondarily in the G2+M cell-cycle phases; (iii) the cytostatic effect of Lov can be specifically inhibited by addition of mevalonate (Mev) (Lov inhibits the synthesis of Mev); (i.v.) removal of Lov from G1-arrested cultures, followed by addition of Mev, resulted in the synchronous recovery of DNA synthesis; and (v) 5-bromo2'-deoxyuridine incorporation expts. revealed that MDBK cells synchronization by Lov can be followed for at least 3 cycles after removal of Lov and addition of Mev. Furthermore, as an application of investigations based on the availability of synchronized MDBK, we showed that bovine herpesvirus-1 gene expression is independent on the cell cycle.

L17 ANSWER 9 OF 12 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001353868 EMBASE
TITLE: Spontaneous reports on drug-induced pancreatitis in Denmark from 1968 to 1999.
AUTHOR: Andersen V.; Sonne J.; Andersen M.
CORPORATE SOURCE: V. Andersen, Medical Department, Viborg County Hospital, 8800 Viborg, Denmark. vandersen@dadlnet.dk
SOURCE: European Journal of Clinical Pharmacology, (2001) Vol. 57, No. 5-6, pp. 517-521. .
Refs: 17
ISSN: 0031-6970 CODEN: EJCPAS
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 2001
Last Updated on STN: 18 Oct 2001

AB Objectives: To present an update on drug-induced pancreatitis reported to the Danish Committee on Adverse Drug Reactions. Design: Retrospective study of spontaneous case reports to the Danish reporting system on adverse drug reactions. Methods: All cases of suspected drug-induced pancreatitis reported to the Danish Committee on Adverse Drug Reactions from 1968 to 1999 were analysed. Three cases were excluded leaving 47 cases for analysis. Results: Drug-induced pancreatitis made up 0.1% of all the reports to the committee from 1968 to 1999. The proportion seemed to increase and was 0.3% during the last 8 years. The 47 cases corresponded to 0.1% of the number of patients discharged due to pancreatic disease (without cancers) per year in Denmark. Serious courses were frequent as indicated by death and hospitalisation being reported in 4 (9%) and 32 (68%) cases, respectively. Death occurred after valproate (two cases), clomipramine (one case) and azathioprine (one case). Definite relationship was stated for mesalazine (three cases), azathioprine (two cases) and simvastatin (one case) on the basis of re-challenge. A possible or probable causality was considered for a further 30 drugs including 5-acetylsalicylic acid agents, angiotensin-converting enzyme inhibitors, estrogen preparations, didanosine, valproate, codeine, antiviral agents used in acquired immunodeficiency syndrome therapy, various lipid-reducing agents, interferon, paracetamol, griseofulvin, ticlopine, allopurinol, lithium and the MMR (measles/ mumps/rubella) vaccination. Conclusion: Drug-induced pancreatitis is rarely reported. The incidence may be increasing and the course is often serious. This is the first report on definite simvastatin-induced pancreatitis. Further studies on the pancreotoxic potential of drugs are warranted.

L17 ANSWER 10 OF 12 EMBASE

ACCESSION NUMBER: 2001315355 EMBASE
TITLE: Drug-associated thrombotic thrombocytopenic purpura-hemolytic uremic syndrome.
AUTHOR: Medina P.J.; Sipols J.M.; George J.N.
CORPORATE SOURCE: P.J. Medina, Department of Pharmacy, College of Pharmacy, Univ. of Oklahoma Hlth. Sci. Center, P.O. Box 26901, Oklahoma City, OK 73190, United States. Patrick-Medina@OUHSC.edu
SOURCE: Current Opinion in Hematology, (2001) Vol. 8, No. 5, pp. 286-293. .
Refs: 83
ISSN: 1065-6251 CODEN: COHEF4
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Sep 2001
Last Updated on STN: 27 Sep 2001

AB Thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS) is an inclusive term describing diverse syndromes of multiple etiologies with the common features of thrombocytopenia and microangiopathic hemolytic anemia. Other organ involvement, including renal failure, neurologic abnormalities, and gastrointestinal symptoms, is common. Adverse reactions to drugs increasingly are reported as a potential cause of TTP-HUS. More than 50 drugs and other substances have been associated with the development of TTP-HUS, but many case reports are difficult to interpret because there is uncertainty regarding the diagnosis of TTP-HUS

and because there is uncertainty regarding the relation of drug exposure to the onset of TTP-HUS. A systematic analysis of reports of drug-associated TTP-HUS will be required to better understand the strength of clinical evidence linking drugs to the etiology of TTP-HUS. In this review, five drugs that have been the subject of the most and the most recent reports of drug-associated TTP-HUS are discussed: mitomycin C, cyclosporine, quinine, ticlopidine, and clopidogrel. The clinical features of TTP-HUS associated with these drugs are different, suggesting two principal mechanisms by which drugs may cause TTP-HUS: dose-related toxicity (mitomycin C, cyclosporine), and immune-mediated reaction (quinine, ticlopidine, clopidogrel). The role of plasma exchange is uncertain, but this treatment is appropriate because of the high mortality and morbidity of drug-associated TTP-HUS. Recognition of a drug-associated etiology in a patient with TTP-HUS is critical to avoid re-exposure and recurrent illness. .COPYRGT. 2001 Lippincott Williams & Wilkins, Inc.

L17 ANSWER 11 OF 12 EMBASE

ACCESSION NUMBER: 1999417502 EMBASE
TITLE: Distinct serum cytokine levels in drug- and measles -induced exanthema.
AUTHOR: Hari Y.; Urwyler A.; Hurni M.; Yawalkar N.; Dahinden C.; Wendland T.; Braathen L.R.; Matter L.; Pichler W.J.
CORPORATE SOURCE: W.J. Pichler, Allergology, Inselspital, CH-3010 Bern, Switzerland. werner.pichler@insel.ch
SOURCE: International Archives of Allergy and Immunology, (1999) Vol. 120, No. 3, pp. 225-229. .
Refs: 12
ISSN: 1018-2438 CODEN: IAAIEG
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Dec 1999
Last Updated on STN: 16 Dec 1999

AB Background: Macular or maculopapular skin reactions are frequent events in drug allergy as well as in viral infections. Clinically, the differentiation may be difficult in the absence of a clear relationship to drug intake or failure to detect virus-specific antibodies of the IgM class. Studies on drug-specific T cell lines and T cell clones isolated from drug-allergic patients have suggested that these cells may represent a significant source of IL-5. On the other hand, viral infections are frequently associated with elevated IFN-γ levels. Objective: Determination of serum-cytokine levels to differentiate between drug- and virally induced skin eruptions. Patients: 18 patients suffering from acute drug allergy and 19 patients with acute measles, rubella or parvovirus infection. Measurements: Cytokine-ELISA (IL-5, IL-4 and IFN-γ) of sera collected during acute drug allergy or during acute measles, rubella or parvovirus infection. Results: In 12/18 patients with drug allergy, IL-5 and/or lL-4 were elevated. A significant correlation (r(Spearman) = 0.84) between IL-5 serum levels and eosinophil counts in the blood was found. No correlation was detected between IL-4 and blood eosinophilia or between IL-4 and IL-5 levels. After remission, IL-5 and IL-4 decreased to undetectable levels. IFN-γ on the other hand was not measurable in patients with drug allergy while elevated IFN-γ serum levels were detected in 17/19 patients with measles, rubella or parvovirus infection; 2 patients with acute virus infection had elevated IL-5, and/or IL-4 and IFN-γ levels. Conclusion: These data underline the distinct pathogenesis of these

morphologically similar exanthemas and suggest that the combined analysis of eosinophilia in the blood, IL-4 and IFN-γ might help in differentiating skin eruptions.

L17 ANSWER 12 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:304342 BIOSIS
DOCUMENT NUMBER: PREV200100304342
TITLE: RhoA signaling is required for RSV-induced syncytia formation and viral filament formation.
AUTHOR(S): Gower, Tara Lynn [Reprint author]; Pastey, Manoj [Reprint author]; Guth, Alex [Reprint author]; Graham, Barney S. [Reprint author]
CORPORATE SOURCE: Vanderbilt University, 1161 21st Ave. South, A-4103 MCN, Nashville, TN, 37212-2582, USA
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A578. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

AB Respiratory syncytial virus (RSV) is an important human pathogen that causes severe lower respiratory infections in children, the immunocompromised, and the elderly. Our laboratory has identified RhoA, a small GTPase, as a cellular ligand for the RSV F (fusion glycoprotein). RhoA controls several cellular processes such as cell cycle progression and cell morphology and migration. In the cell, RhoA activates the formation of actin stress fibers and focal adhesions as well as gene transcription. We have also shown that RhoA and its downstream signaling cascades are activated by RSV infection. Based on these findings, we asked whether RhoA activation and signaling are required for RSV replication. There are several reagents available to inhibit RhoA activation and signaling. These inhibitors include: Rho Kinase inhibitor, Y-27632, which prevents RhoA induced signaling through Rho Kinase; C3 toxin which ADP-ribosylates RhoA and inactivates its signaling capabilities; Lovastatin and GGTI-298 which inhibit protein isoprenylation, thereby preventing the localization of RhoA to the plasma membrane; Cytochalasin D, which inhibits actin polymerization. Using these inhibitors, we have shown that RhoA signaling and actin polymerization are required for RSV-induced plaque formation and cell-to-cell fusion. Interestingly, RSV-infected cells form filamentous protrusions that are coated with the viral envelope proteins, F and G. We have also shown that inhibiting RhoA signaling inhibits the formation of viral filaments by scanning electron microscopy. Based on these data, we conclude that RhoA signaling is required for RSV-induced filaments, and filaments play an important role in RSV-induced cell-to-cell fusion and syncytia formation.